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REPLY BRIEF UNDER 37 C.F.R. § 1.193(b)(1)

This Reply Brief is filed pursuant to 37 CFR § 1.193(b)(1) and is filed in response to the Examiner's Answer of March 6, 2007, the Examiner's Answer being in response to an Appeal Brief filed November 17, 2006.

APPELLANTS' CLAIMED INVENTION MEETS THE REQUIREMENTS FOR PATENTABILITY

As discussed in the Appeal Brief filed November 17, 2006, the specification meets the requirements of 35 U.S.C. § 112 and fully describes and enables the rejected claims. Thus, it is respectfully requested that the rejections be reversed.

Claims 1-3, 9-12, 17-19, 43, 46, 49, 52, and 55-64 stand rejected under 35 U.S.C. § 112, first paragraph as not enabled and lacking written description. The Examiner's rejections and arguments have been fully addressed in Appellants' Appeal Brief filed November 17, 2006. Those arguments are incorporated herein by reference. This reply will focus on the correct standard to be used to evaluate a specification for enablement and written description under 35 U.S.C. § 112, first paragraph and how Appellants have met the proper standard.

THE EXAMINER IS USING THE WRONG STANDARD IN EVALUATING THE SPECIFICATION FOR ENABLEMENT

The Examiner rejects the present claims and argues throughout the Examiner's Answer that the specification fails to provide guidance for the full scope of the claimed invention. Throughout the Answer, the Examiner's central argument is that the specification does not demonstrate every nucleic acid sequence that falls within the scope of the claims. The Examiner reasons that:

> Because nucleic acids that have 90% identity to the 3621 nucleotide long SEQ ID NO:1 would have up to 362 nucleotide substitutions, they could encode proteins with up to 362 amino acid substitutions; these proteins would have 70% identity to the 1206 amino acid long SEQ ID NO:2. The specification provides no guidance for which 362 amino acids to substitute, and still maintain Coleopteran pesticidal activity.

Examiner's Answer, page 5, line 19 – page 6, line 1.

On page 8 of the Answer, the Examiner states:

> Given the claim breath [*sic*], unpredictability, and lack of guidance, as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids with 90% identity to SEQ ID NO:1. a trail [*sic*] and error approach to making the claimed nucleic acids may require one to make all possible single amino acid substitutions in SEQ ID NO:1. Making all possible single amino acid substitutions in an 3621 nucleotide long nucleic acid like that of SEQ ID NO:1 would require making and analyzing 19^{3621} nucleic acids (or 2.3×10^{4630}) nucleic acids . . . Because nucleic acids that have 90% identity to SEQ ID NO:1 would have up to 362 nucleotide substitutions, many more than 19^{3621} nucleic acids would need to be made and analyzed without further guidance.

Examiner's Answer, page 8, lines 4-14.

The Examiner concludes on page 9 of the Examiner's Answer that "[g]iven the claim breath [*sic*], unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims."

Likewise, in responding to Appellants' arguments regarding enablement, the Examiner continues to require that every possible substitution be taught in the specification. For example, on page 11, the Examiner argues that "[t]he guidance fails to sufficiently teach which 362 amino

acid substitutions to make in SEQ ID NO:2, given the unpredictability in making amino acid substitutions in *Cry* proteins." See, lines 11-13.

Regarding the variants that are described in the specification and set forth in Appendix A of Appellants' Brief, the Examiner states,

> Further, even if one were to consider SEQ ID NO:20 and 16 as teaching proteins with 52% and 56% identity to SEQ ID NO:2, they would not teach how to make proteins with 362 amino acid substitutions over the entire length of SEQ ID NO:2.
>
> Third, the 4 amino acid, long substitutions/insertions at amino acid 164 of SEQ ID NO:2 are a teaching of the variants, but the variants do not teach the full scope of the claimed variants. One of skill in the art would not consider the sequences as teaching, which 181, 217, 253 or 362 amino acids to substitute in SEQ ID NO:2. . . Thus, SEQ ID NO:3 cannot provide all the necessary guidance for making nucleic acids with 90% identity to SEQ ID NO:1 and encoding a protein with 362 amino acid substitutions relative to SEQ ID NO:2, as encompassed by the full scope of the claims.

Page 14, lines 5-11 and 16-19.

In response to Appellants' arguments that the Examiner overlooks the support in the specification for enablement of the claims, the Examiner notes that "the guidance provided in the specification is not sufficient to teach how to make nucleic acids within the full scope of the claims." Page 16, lines 6-7. The Examiner goes on to argue that:

> Making the nucleic acids would require undue experimentation, because the specification does not provide sufficient guidance as to which 362 amino acid substitutions can be made in SEQ ID NO:2. Thus, one would need to randomly make nucleic acids encoding proteins with 362 amino acid substitutions and test them. Because the lack of guidance in the specification means this would require trail [*sic*] and error experimentation, because of the likelihood of protein inactivation (see Guo et al, pg 9209, right column, paragraph 2), and because of the unpredictability of amino acid interactions in *Cry* proteins (de Maagd et al, 1999, pg 4369, column 1, paragraph 1), this experimentation would be undue.

Page 17, lines 17-24.

The Examiner maintains that the specification is not sufficient for one to make and use the invention because, "[m]aking the nucleic acids would require undue experimentation because

the specification does not provide sufficient guidance as to which 362 amino acid substitutions can be made in SEQ ID NO:2." Page 17, lines 17-19.

Likewise when the Examiner considers SEQ ID NO:3, which has 92% identity to SEQ ID NO:1, the Examiner argues that SEQ ID NO:3 does not provide sufficient guidance for making nucleic acids with 90% identity to SEQ ID NO:1 and encoding a protein with 362 amino acid substitutions relative to SEQ ID NO:2. See, page 18, lines 7-9.

Appellants noted in their Brief that at the time of filing it was routine to mutate amino acids in a protein and test for activity. In response, the Examiner states that "although point mutations and substitutions of a few amino acids have been made in *Cry* proteins, no one has substituted, 362, 253, 217 or 181 amino acids of a Cry protein, as encompassed the [*sic*] claimed nucleic acids." Page 19, lines 11-13.

On page 20, second paragraph, of the Examiner's Answer, the Examiner asserts that:

> However, the claims are not limited to changes made only in the deleted region, of [*sic*] such changes even can be made. The 5 conserved blocks and 3 domains in the N-terminal half of the protein (the non-deleted region) are not also sufficient to teach which 362 amino acid substitutions to make over the full length of the protein, as encompassed by the full scope of the claims.

In response to Appellants arguments that the cited references support the position that making changes in a polypeptide and testing for activity are routine, the Examiner counters that: "[h]owever, the guidance and insights are not sufficient for making nucleic acids encoding Coleopteran pesticidal proteins with 362 amino acid substitutions distributed over the entire length of SEQ ID NO:2." Page 22, lines 1-3. Regarding the Li reference, the Examiner notes that:

> Li et al [*sic*] only provides [*sic*] guidance for making truncations and insertion of chymotrypsin cleavage sites; Li et al [*sic*] do not provide guidance for making 181, 217, 253 or 362 amino acid substitutions in a 1206 amino acid protein. . . Further, the instant inventors did not use Li et al [*sic*] to make 181, 217, 253 or 362 amino acid substitutions in a 1206 amino acid protein to create a Coleopteran pesticidal protein.

Page 22, lines 6-8 and 13-14.

Even regarding the disclosed natural variant (SEQ ID NO:3) of SEQ ID NO:1, which shares 92% identity to SEQ ID NO:1, the Examiner discounts the teaching and indicates that, "SEQ ID NO:3 does not encode a protein that had 362 amino acid substitutions relative to SEQ ID NO:2 – it encodes a protein that has only about 132 amino acid substitutions relative to SEQ ID NO:2. Thus, it does not provide guidance for making nucleic acids within the full scope of the claims." Page 22, lines 16-19.

Continuing throughout the Examiner's Answer, the recurring argument is that Appellants have not taught how to make nucleic acids that encode Coleopteran pesticidal proteins with 362 amino acid substitutions relative to SEQ ID NO:2. See, page 23, lines 3-4, lines 13-17, and lines 20-21; page 24, lines 11-13 and lines 19-20; page 25, lines 20-21; page 26, lines 6-7; page 27, lines 6-7; and page 28, lines 3-6.

The Examiner's rejection lies in the fact that every possible nucleic acid encompassed by the claims is not disclosed in the specification. By the Examiner's arguments, the only way to enable the claims is to demonstrate every possible embodiment that falls within the scope of the claims. This is not the proper standard for evaluating enablement.

THE CORRECT ENABLEMENT STANDARD

The enablement section of 35 U.S.C. § 112, first paragraph, "requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970). It is well established that the specification does not have to exemplify every embodiment that falls within the scope of the claims. "That *some* experimentation may be required is not fatal, the issue is whether the amount of experimentation required is 'undue.'" *In re Vaeck*, 947 F.2d at 488. In order to determine whether the present claims are enabled, an analysis of the teachings of the specification must be performed as well as an inquiry into the knowledge of persons of ordinary skill in the art. *In re Bowen*, 492 F.2d 859, 861 (C.C.P.A. 1974).

It is improper to limit the scope of a claimed invention to that which is disclosed in working examples. See *In re Anderson*, 471 F.2d 1237, 1240-1241 (C.C.P.A. 1973), where the court held "we do not regard section 112, first paragraph, as requiring a specific example of

everything *within the scope* of a broad claim. . . . What the Patent Office is here apparently attempting is to limit all claims to the specific examples, notwithstanding the clear disclosure of a broader invention. This it may not do." To satisfy the enablement requirement Applicants need not demonstrate that every nucleotide sequence encompassed by the claims could be used to successfully practice the invention, such that no experimentation would be required. According to the applicable case law, the appropriate test of enablement is not whether experimentation is necessary to make and use an invention, but rather if experimentation is necessary, whether it is undue. *In re Angstadt*, 537 F.2d 498 (C.C.P.A. 1976). In fact, a considerable amount of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance in which the experimentation should proceed. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

Enablement has been found lacking in cases where the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. See, e.g., *In re Goodman*, 11 F.3d 1046, (Fed. Cir. 1993); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991); *In re Vaeck*, 947 F.2d 488, (Fed. Cir. 1991). In contrast to the Examiner's assertion, the test is not merely quantitative. A considerable amount of experimentation is permissible, if the experimentation is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed, to enable the determination of how to practice an embodiment of the claimed invention.

THE SPECIFICATION MEETS THE CORRECT STANDARD

A. Numerous examples are provided in the specification

In the present specification numerous examples of nucleic acids that fall within the scope of the claims are provided. A summary of the sequences presented in the application were presented in Table form for the Examiner's convenience in the Reply Brief filed February 23, 2006, and in the amendment filed August 11, 2006. A copy of the Table was provided as Evidence Appendix A with the Appeal Brief filed by Appellants on November 17, 2006. The Table contains a listing of the sequences set forth in the specification and sequence identity analysis of the sequences with SEQ ID NO:1.

As summarized in the Table, the specification provides fourteen (14) variants of SEQ ID NO:1, which share between 38% and 92% identity across the full length of SEQ ID NO:1, all of which encode proteins with pesticidal activity against Coleopterans. When local alignments are preformed between the truncated variants and nucleotides 1 to 2097 of SEQ ID NO:1, the percent identity of these truncated variants to SEQ ID NO:1 ranges between 100% to 68% sequence identity. As multiple nucleic acid variants encoding active pesticidal proteins have been provided, all of which have a relationship to SEQ ID NO:1 well below the percent identities recited in the instant claims, the claims of the present invention are enabled.

SEQ ID NO:1 comprises 3621 nucleotides. SEQ ID NO:3 provided in the specification is a natural variant of SEQ ID NO:1 that exhibits 92% identity to SEQ ID NO:1 and encodes a protein retaining Coleopteran pesticidal activity. Numerous other examples are discussed in Appellants' Appeal Brief. Accordingly, the data in the specification provides clear guidance to one of skill in the art that nucleic acid variants having at least 90%, at least 93%, at least 94%, and at least 95% sequence identity to SEQ ID NO:1 and which encode pesticidal proteins can be readily made.

Additionally, the specification teaches those skilled in the art how to make the claimed nucleotide sequences and test those sequences for the required activity. The specification provides: nucleotide sequences that fall within the scope of the claims (see, for example, pages 11, 12, 13, 14, 18, 19, 25, and 65); guidance regarding alterations that allow the protein to retain pesticidal activity (see, for example, pages 11, 12, 13, 14, and 18-20); methods for assaying the pesticidal activity of proteins (pages 8 and 29, Example 4, Example 6, and Example 7); a discussion of Cry-8-like δ-endotoxins (SEQ ID NO:2 is a Cry-8-like δ-endotoxin) (pages 24-25); guidance for determining percent identity of sequences (pages 33-38); and specific mutations that fall within the scope of the claimed invention (pages 11, 12, 13, 14, 18, 19, and 25; and Examples 4 and 6).

Accordingly, a reasonable amount of guidance is provided in the specification for making variants that fall within the scope of the claims.

B. The work required to practice the invention throughout its scope is routine

Importantly, the work required to practice the invention throughout its scope would be considered routine. To make the claimed variants of SEQ ID NO:1, a person skilled in the art would only need to utilize standard molecular biology and mutagenesis techniques and routine screening assays for pesticidal activity; all of which are not only described and exemplified in the specification but were well known in the art at the time of the invention. In fact, the references cited by the Examiner and attached as Exhibits to Appellants' Appeal Brief demonstrate that at the time of the invention it was routine to mutate amino acids in a polypeptide and then test the altered polypeptide for activity. The Lazar reference published in 1988 (Evidence Appendix B) and the Hill reference published in 1998 (Evidence Appendix C), both demonstrate that one of skill in the art well before 2000, the priority date of the present application, could make substitutions in polypeptide sequences and test for activity. Nothing more is required in the present application.

The de Maagd, Tounsi, and Angsuthanasombat references all make substitutions in Cry proteins and then test for activity. This is all that is required to test sequences that fall within the scope of the claims. The de Maagd reference was published in 1999 (Evidence Appendix D) and the Angsuthanasombat reference was published in 2001 (Evidence Appendix E). Again, these references demonstrate that one of skill in the art could make sequences having at least 90%, at least 93%, at least 94%, or at least 95% sequence identity to a known sequence and test for activity of the encoded protein at the time of the invention.

One of skill in the art would readily understand whether a particular nucleotide sequence has at least 90%, at least 93%, at least 94%, and at least 95% identity to SEQ ID NO:1 as required by the claims. In addition, the assays disclosed in the specification provide sufficient guidance for one skilled in the art to determine whether a particular nucleotide sequence encodes a protein with Coleopteran pesticidal activity, and thus falls within the scope of the claims. Accordingly, the specification meets the enablement requirement and the rejection should be overturned.

C. The specification satisfies the *Wands* factors for enablement

The holding of *Wands* does not require that Appellants provide as working examples every variant of SEQ ID NO:1 that could be used to practice the present invention. Rather, *Wands* sets out factors to be considered in determining whether undue experimentation is required to make and use the invention. These factors include: the quantity of experimentation necessary, the amount of guidance provided in the specification, the presence of working examples of the invention in the application, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability in the art, and the breadth of the claimed invention. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Examiner argues that the quantity of experimentation necessary is undue. However, the Examiner bases this conclusion on the wrong assumption that one would have to make and test every nucleic acid sequence that falls within the scope of the claim. In contrast, one skilled in the art would understand whether a particular nucleic acid has at least 90%, at least 93%, at least 94%, and at least 95% sequence percent identity to SEQ ID NO:1 and encodes a polypeptide having the required pesticidal activity as set forth in the claims. With the guidance provided in the specification and in the art, and following the examples set forth in the specification, there is sufficient guidance for one skilled in the art to determine whether a particular nucleic acid is within the scope of the claims. As demonstrated in the present specification and in the cited art, mutating a nucleic acid sequence and testing for activity of the encoded protein is routine and one is readily able to ascertain whether the nucleic acid sequence falls within the scope of the claim at the end of the analysis. Accordingly, it would not require undue experimentation for one skilled in the art to make and use the claimed invention.

The law is clear, as set forth in the Appeal Brief, that where a generic claim to a genetic sequence does not encompass all possible analogs or variants of a DNA sequence, it may be possible to provide an enabling disclosure by a sufficient showing of how to make and use analogs that are similar to a disclosed sequence. The present specification clearly meets that standard.

In summary, for all the reasons set forth above, the present claims are fully enabled and the rejection of the claims under 35 U.S.C. §112, first paragraph as lacking enablement should be

reversed. However, as noted in the Appeal Brief, should the Board disagree, claims requiring 93%, 94%, and 95% sequence identity are narrower in scope and thus should be considered separately.

THE EXAMINER IS USING THE WRONG STANDARD IN EVALUATING THE SPECIFICATION FOR WRITTEN DESCRIPTION

Regarding the written description rejection, the Examiner argues that the specification does not teach every modification that can be made that fits within the full scope of the claims. Using the same arguments that are set forth in the enablement rejection, the Examiner reasons that because every variant that falls within the scope of the claims has not been described in the specification, the specification does not meet the requirements for written description.

On page 9, the Examiner sets forth:

> The claim is directed to a genus of nucleic acids that have 90%, 93%, 94%, or 95% identity to SEQ ID NO:1. Nucleic acids that have 90%, 93%, 94%, or 95% identity to SEQ ID NO:1 would have up to 362 nucleotide substitutions, they could encode proteins with up to 362, 253, 217 or 181 amino acid substitutions relative to the to the [*sic*] 1206 amino acid long SEQ ID NO:2.

Examiner's Answer, page 9, lines 16-20.

Regarding the sequences set forth in the specification and summarized in the Table, the Examiner argues that "the sequences in the Table do not describe the structure of nucleic acid [*sic*] within the full scope of the claims. No nucleic acid with identity to SEQ ID NO:1 and that encodes a Coleopteran pesticidal protein with 70% identity to the original protein has been described." Page 29, lines 1-3. Further the Examiner indicates that "[t]he specification has not described the structure of any nucleic acid with 90% identity to SEQ ID NO:1 and that encodes a Coleopteran pesticidal protein with 362 amino acid substitutions relative to SEQ ID NO:2, much less the full scope of such nucleic acids." Page 29, lines 7-10. The Examiner reasons that "a representative number of nucleic acids that have 90%, 94% or 95% identity to SEQ ID NO:1 and up to 362, 253, 217 or 181 amino acid substitutions, respectively, relative to the to the [*sic*] 1206 amino acid long SEQ ID NO:2 are not described.

Again at page 30, lines 15-18, the Examiner discounts the nucleic acid variants provided in the specification and asserts:

> However, these variants are very similar to one another. The full scope of nucleic acids encompassed by the claims are not described. For example, the specification does not describe the structure of any nucleic acid encoding a coleopteran pesticidal protein with 362 amino acid substitutions distributed over the full length of SEQ ID NO:2.

Regarding the narrower claims drawn to 93%, 94%, or 95%, the Examiner maintains the same reasoning that "the specification also does not describe the structure of nucleic acids with 93%, 94% or 95% identity to SEQ ID NO:1 and that encode Coleopteran pesticidal proteins with up to, [*sic*] 253, 217 or 181 amino acid substitutions relative to SEQ ID NO:2. Page 31, lines 10-12.

The Examiner's reasoning is that Appellants were not in possession of the invention and thus has not satisfied the written description requirement because they have not shown every nucleic acid that falls within the scope of the claims. This is not the proper standard for determining whether the written description requirement has been met.

THE PROPER STANDARD TO DETERMINE WHETHER THE WRITTEN DESCRIPTION REQUIREMENT HAS BEEN MET

In order to satisfy the written description requirement of 35 U.S.C. §112, the applicant must reasonably convey to one skilled in the art that the applicant was in possession of the claimed subject matter at the time the application was filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). Every species encompassed by the claimed invention, however, need not be disclosed in the specification to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. The Federal Circuit has made it clear that sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320 1323 (Fed. Cir. 2000) ("[O]ne skilled in the art, reading the original disclosure, must immediately discern the limitations at issue in the claims.").

Moreover, the "Guidelines for Examination of Patent Applications Under 35 U.S.C. §112, ¶ 1, 'Written Description' Requirement" state that a genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying

characteristics , *i.e.* structure or other physical and/or chemical properties." This is in accordance with the standard for written description set forth in *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing *Fiers v. Revel* 984 F.2d 1164, 1171 (Fed. Cir. 1993). In *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956 (Fed. Cir. 2002), the Federal Circuit adopted the PTO standard for written description, stating:

> [U]nder the Guidelines, the written description requirement would be met . . . if the functional characteristics of [a genus of nucleic acids or polypeptides] were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed. We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement."

The Examiner's approach to determining whether a specification has an adequate written description is to view the specification in terms of whether every possible nucleic acid that falls within the scope of the claims is provided. This approach is improper. The written description inquiry should focus on whether the specification reasonably conveys to one skilled in the art whether the applicant invented the claimed subject matter. As the Federal Circuit has established, where the invention is directed to the use of nucleic acids having specific structural and biological properties, the written description requirement may be satisfied if there is a correlation between the structure of a compound and its function. *Vas-Cath, Inc. v. Mahurkar*, 935 F2d 1555, 1563 (Fed. Cir. 1991).

With respect to the present claims, the specification provides nucleic acid sequences that fall within the scope of the claims. The rejected claims drawn to variants recite nucleotide sequences having a specified percent identity to a *disclosed* nucleotide sequence. The present claims further recite functional characteristics that distinguish the sequences of the claimed genus. Specifically, the claims recite that the claimed nucleotide sequences encode a polypeptide having pesticidal or insecticidal activity. Pesticidal activity and insecticidal activity are clearly defined in the application. The specification provides the requisite correlation

between the structure of the claimed nucleic acids and its function. See, *University of Rochester v. G.D. Searle & Co.*, 358 F. 3d 916, 925 (Fed. Cir. 2004), and *Enzo Biochem Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324 (Fed. Cir. 2002). Therefore, both the structural and functional properties that characterize the genus of sequences that can be used to practice the invention are specifically recited in the claims. The sequences that fall within the scope of the claims can readily be identified by the methods set forth in the specification.

As in the rejection for lack of enablement, the Examiner is reading limitations into the claims that are not required. The claims only require a nucleic acid comprising a nucleotide sequence having at least 90%, 93%, 94%, or 95% sequence identity to the nucleotide sequence set forth in SEQ ID NO:1, wherein said nucleotide sequence encodes a polypeptide which is pesticidal for at least one pest belonging to the order Coleoptera. The claims do not require that the encoded polypeptide have 362 or any amount of amino acid substitutions. The Examiner, as shown above, focuses on the fact that a nucleotide sequence having 90% identity to SEQ ID NO:1 could encode a protein having 362 substitutions in SEQ ID NO:2. In fact, many nucleotide sequences having 90% identity or less to SEQ ID NO:1 can be envisioned that encode a polypeptide identical to SEQ ID NO:2 or with a few amino acid differences (see SEQ ID NO:9, which encodes a truncated SEQ ID NO:2 but shares only 68% local sequence identity to SEQ ID NO:1.)

A determination of whether a given nucleic acid is within the scope of the claims only requires providing a variant sequence and testing the encoded protein for activity. The claims provide a structure and correlate the structure with a biological property. This meets the requirement set forth by the Federal Circuit in holding that the written description requirement might be satisfied if there is a correlation between the structure of a compound and its function. *University of Rochester v. G.D. Searle & Co.*, 358 F. 3d 916, 925 (Fed. Cir. 2004); *Enzo Biochem Inc. v. Gen-Probe Inc.*, 296 F. 3d 1316, 1324 (Fed. Cir. 2002).

Appellants submit that the relevant identifying structural and functional properties of the genus of sequences of the present invention would be clearly recognized by one of skill in the art. Consequently, Appellants were in possession of the invention at the time the application was

filed, and the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of written description should be withdrawn.

EXAMPLE 14 OF THE WRITTEN DESCRIPTION GUIDELINES IS ON POINT

The Examiner disagrees with Appellants and argues that Example 14 of the Written Description Guidelines is different from that in the present case. However, Example 14 is on point with the facts of the present case. Example 14 reviews a claim drawn to "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B." Written Description Guidelines, page 53. In the example, the specification discloses a single protein that catalyzed the reaction and contemplates but does not exemplify variants of the proteins wherein the variant can have substitutions, deletions, insertions, and additions. The specification indicates that procedures for making variants are routine in the art and provides an assay for detecting the catalytic activity of the protein.

In the analysis, the Guidelines conclude that the **single disclosed species** is enough since the specification indicates that the genus of proteins that must be variants of SEQ ID NO:3 does not have substantial variation since all of the variants must possess the specified catalytic activity and have at least 95% identity to the reference sequence, SEQ ID NO:3. The Guidelines further note that the **single species is representative** of the genus because all members have at least 95% structural identity with the reference compound and because an assay was provided for identifying all of the claimed variants. The conclusion states, "[t]he disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention." Written Description Guidelines, page 55.

In the present case, the specification provides a reference nucleic acid, SEQ ID NO:1. The genus of nucleic acids being claimed must be variants of SEQ ID NO:1 and must encode a protein possessing pesticidal activity. In addition, in the present case variants to the reference nucleic acid are disclosed in the specification. The specification provides fourteen (14) variants of SEQ ID NO:1 that share between 38% and 92% identity across the full length of SEQ ID NO:1 and which encode polypeptides having the required pesticidal activity. When local alignments are performed between the truncated variants and nucleotides 1 to 2097 of SEQ ID

NO:1, the percent identity of the active variants to SEQ ID NO:1 ranges between 100% to 68% sequence identity. Multiple variants have been provided which have a relationship to SEQ ID NO:1 well below the percent identities recited in the instant claims and which encode polypeptides that retain the required pesticidal activity. The specification further provides an assay for testing whether the encoded polypeptide variants have the required activity. See, for example, pages 13 and 61, as well as Examples 1-3 of the instant specification. In fact, the assay is exemplified in the Experimental Section (Examples 1-3) of the specification where the variants are tested for activity.

Accordingly, Example 14 of the Written Description Guidelines is applicable to the present case. Since the present specification provides more than Example 14 requires, the claims are fully described in the specification, and the rejection of the claims as not meeting the written description requirement should be overturned.

CONCLUSION

Appellants maintain that the Examiner has failed to carry her burden of establishing that the claims are not patentable because she has (a) failed to establish that it would require undue experimentation to practice the claimed invention and (b) failed to prove that the application does not adequately describe the claimed invention. For these reasons, presented in Appellant's Brief and summarized herein, Appellants respectfully request that the rejections be reversed.

Respectfully submitted,

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